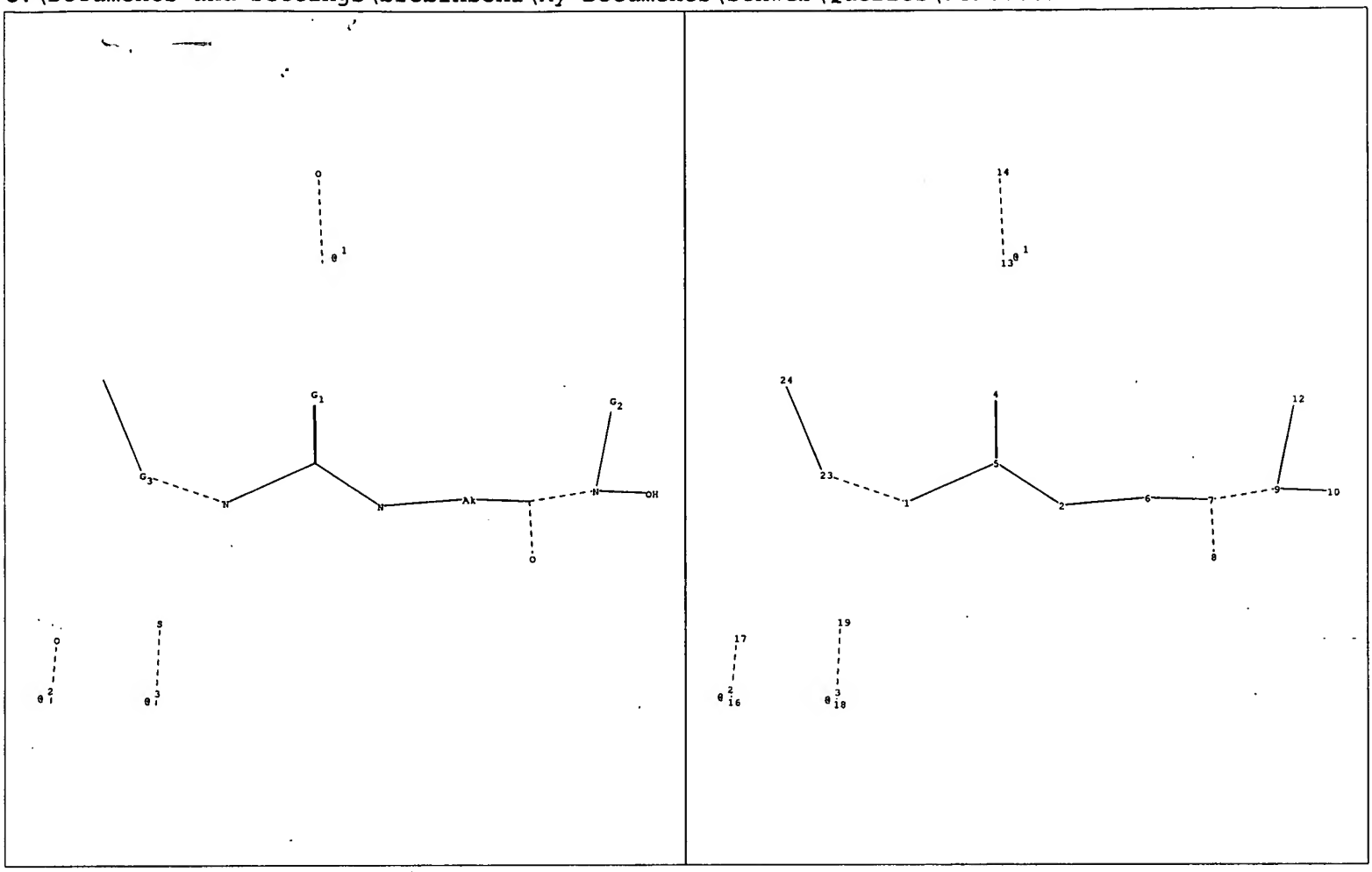
C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\afnb.str



chain nodes :
1 2 4 5 6 7 8 9 10 12 13 14 16 17 18 19 23
ring/chain nodes :
24
chain bonds :
1-5 1-23 2-5 2-6 4-5 6-7 7-8 7-9 9-10 9-12 13-14 16-17 18-19 23-24
exact/norm bonds :
1-5 1-23 2-5 2-6 4-5 6-7 7-8 7-9 9-10 9-12 13-14 16-17 18-19 23-24

G1:O,S,N

G2:Ak,H,[*1]

G3:SO2,[*2],[*3]

Match level :
1:CLASS 2:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS
12:CLASS 13:CLASS 14:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 23:CLASS 24:CLASS

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1612bxr

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 29	JAN 02	STN pricing information for 2008 now available
NEWS 30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

Updated Search

```
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:25:14 ON 23 JAN 2008

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 12:25:19 ON 23 JAN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   22 JAN 2008  HIGHEST RN 1000503-75-2
DICTIONARY FILE UPDATES:  22 JAN 2008  HIGHEST RN 1000503-75-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\afnb.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.



Updated Search
```

```
=> s l1
SAMPLE SEARCH INITIATED 12:29:16 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        50 TO ITERATE

100.0% PROCESSED       50 ITERATIONS                              2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          576 TO     1424
PROJECTED ANSWERS:               2 TO      124

L2             2 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 12:29:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      1154 TO ITERATE

100.0% PROCESSED     1154 ITERATIONS                             99 ANSWERS
SEARCH TIME: 00.00.01

L3             99 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             181.12     181.33

FILE 'HCAPLUS' ENTERED AT 12:29:23 ON 23 JAN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 23 Jan 2008  VOL 148 ISS 4
FILE LAST UPDATED: 22 Jan 2008  (20080122/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l3
L4             20 L3

=> s l4 and lim, z?/au
               40 LIM, Z?/AU
L5              1 L4 AND LIM, Z?/AU



Updated Search
```

=> d l5, ibib abs hitstr, 1

L5 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN

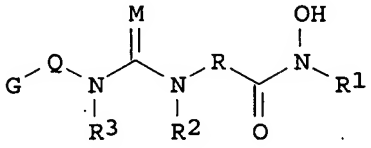
ACCESSION NUMBER:	2005:395258 HCAPLUS
DOCUMENT NUMBER:	142:446921
TITLE:	A preparation of acylurea- and sulfonylurea-connected hydroxamates, useful as histone deacetylase (HDAC) inhibitors
INVENTOR(S):	Lim, Ze-Yi; Wang, Haishan; Zhou, Yan
PATENT ASSIGNEE(S):	Sbio Pte. Ltd., Singapore
SOURCE:	PCT Int. Appl., 145 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

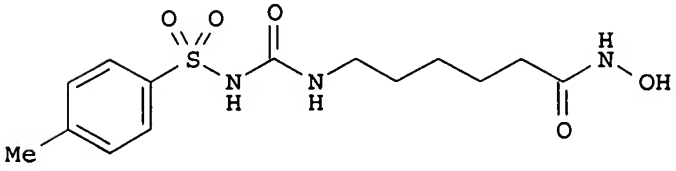
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005040101	A1	20050506	WO 2004-SG353		20041026
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004284030	A1	20050506	AU 2004-284030		20041026
CA 2543570	A1	20050506	CA 2004-2543570		20041026
EP 1685094	A1	20060802	EP 2004-775672		20041026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
JP 2007509930	T	20070419	JP 2006-537946		20041026
MX 2006PA04735	A	20061214	MX 2006-PA4735		20060427
PRIORITY APPLN. INFO.:			US 2003-514013P	P	20031027
			WO 2004-SG353	W	20041026

OTHER SOURCE(S): CASREACT 142:446921; MARPAT 142:446921

GI



I



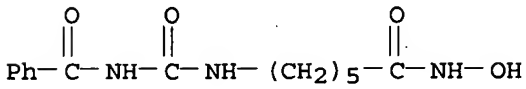
II

Updated Search

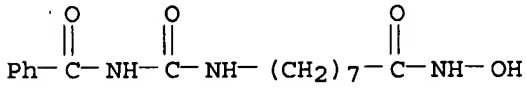
AB The invention relates to a preparation of acylurea- and sulfonylurea-connected hydroxamates of formula I [wherein: R is a linking moiety; R1 is H, alkyl, or acyl; M is O, S, NH, NOH, or N(alkyl), etc.; R2 and R3 are independently selected from H, halogen, alkyl, alk(en/yn)yl, or heteroalkyl, etc.; Q is SO2, C(O), or C(S); G is (cyclo)alkyl, (hetero)aryl, or arylalkyl, etc.], useful as HDAC inhibitors. For instance, hexanoic acid derivative II [IC50 (μM): HDAC1 - >100, HDAC8 - 0.79] was prepared from Me 6-aminohexanoate hydrochloride and phenylsulfonyl isocyanate with a yield of 58%.

IT 851365-34-9P 851365-36-1P 851365-37-2P
851365-38-3P 851365-39-4P 851365-40-7P
851365-41-8P 851365-43-0P 851365-45-2P
851365-46-3P 851365-48-5P 851365-49-6P
851365-50-9P 851365-70-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acylurea- and sulfonylurea-connected hydroxamates useful as HDAC enzyme inhibitors)

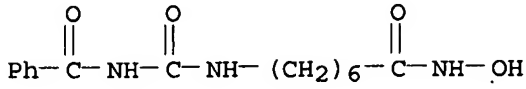
RN 851365-34-9 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl]amino]carbonyl]- (CA INDEX NAME)



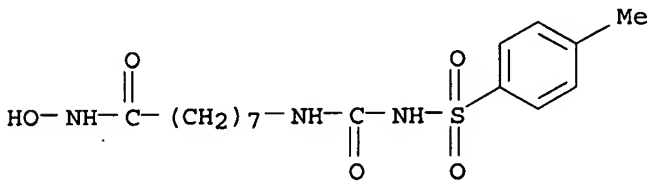
RN 851365-36-1 HCAPLUS
CN Benzamide, N-[[[8-(hydroxyamino)-8-oxooctyl]amino]carbonyl]- (CA INDEX NAME)



RN 851365-37-2 HCAPLUS
CN Benzamide, N-[[[7-(hydroxyamino)-7-oxoheptyl]amino]carbonyl]- (CA INDEX NAME)

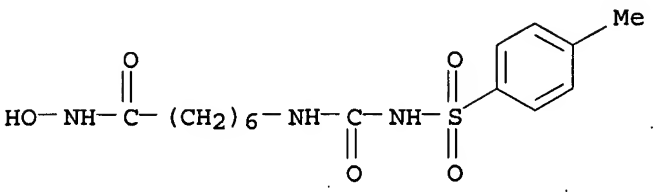


RN 851365-38-3 HCAPLUS
CN Octanamide, N-hydroxy-8-[[[[(4-methylphenyl)sulfonyl]amino]carbonyl]amino]- (CA INDEX NAME)

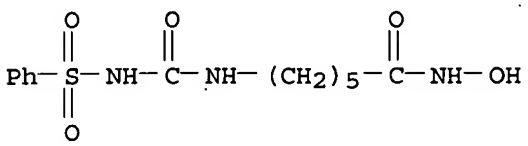


Updated Search

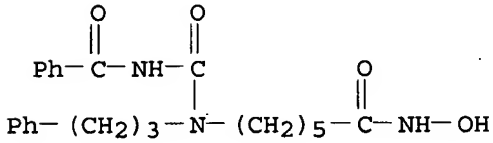
RN 851365-39-4 HCAPLUS
CN Heptanamide, N-hydroxy-7-[[[[(4-methylphenyl)sulfonyl]amino]carbonyl]amino]- (CA INDEX NAME)



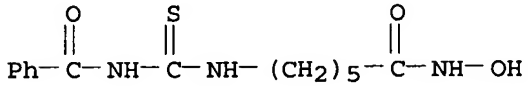
RN 851365-40-7 HCAPLUS
CN Hexanamide, N-hydroxy-6-[[[(phenylsulfonyl)amino]carbonyl]amino]- (CA INDEX NAME)



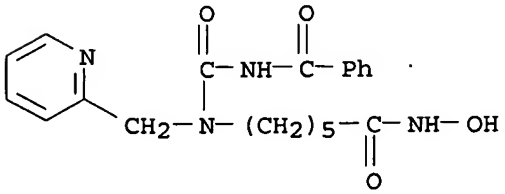
RN 851365-41-8 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl](3-phenylpropyl)amino]carbonyl]- (CA INDEX NAME)



RN 851365-43-0 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl]amino]thioxomethyl]- (CA INDEX NAME)



RN 851365-45-2 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl](2-pyridinylmethyl)amino]carbonyl]- (CA INDEX NAME)

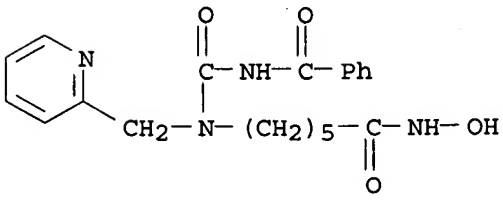


Updated Search

RN 851365-46-3 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl](2-pyridinylmethyl)amino]carbonyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

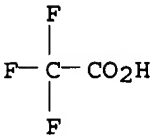
CM 1

CRN 851365-45-2
CMF C20 H24 N4 O4

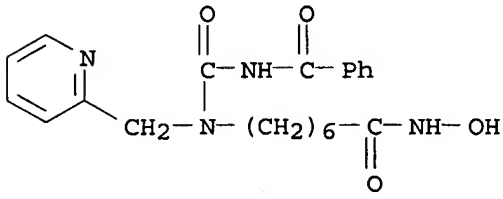


CM 2

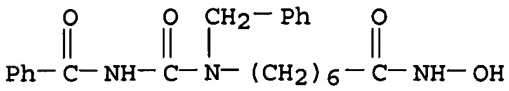
CRN 76-05-1
CMF C2 H F3 O2



RN 851365-48-5 HCAPLUS
CN Benzamide, N-[[[7-(hydroxyamino)-7-oxoheptyl](2-pyridinylmethyl)amino]carbonyl]- (CA INDEX NAME)

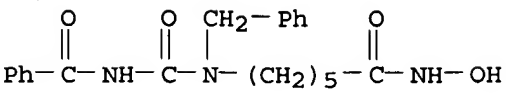


RN 851365-49-6 HCAPLUS
CN Benzamide, N-[[[7-(hydroxyamino)-7-oxoheptyl](phenylmethyl)amino]carbonyl]- (CA INDEX NAME)

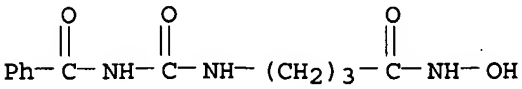


RN 851365-50-9 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl](phenylmethyl)amino]carbonyl]- (CA INDEX NAME)

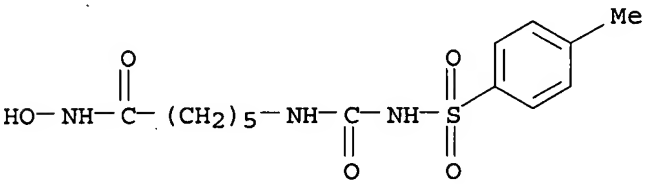
Updated Search



RN 851365-70-3 HCAPLUS
CN Benzamide, N-[[[4-(hydroxyamino)-4-oxobutyl]amino]carbonyl]- (CA INDEX NAME)



IT 851365-24-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of acylurea- and sulfonylurea-connected hydroxamates useful as HDAC enzyme inhibitors)
RN 851365-24-7 HCAPLUS
CN Hexanamide, N-hydroxy-6-[[[[(4-methylphenyl)sulfonyl]amino]carbonyl]amino]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 12:25:14 ON 23 JAN 2008)

FILE 'REGISTRY' ENTERED AT 12:25:19 ON 23 JAN 2008
L1 STRUCTURE UPLOADED
L2 2 S L1
L3 99 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 12:29:23 ON 23 JAN 2008
L4 20 S L3
L5 1 S L4 AND LIM, Z?/AU

=> s l4 not l5
L6 19 L4 NOT L5

=> s l6 and wang, h?/au
44077 WANG, H?/AU
L7 0 L6 AND WANG, H?/AU

=> s l6 and zhou, y?/au

Updated Search

18479 ZHOU, Y?/AU
L8 0 L6 AND ZHOU, Y?/AU

=> d l6, ibib abs fhitstr, 1-19

L6 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1447760 HCAPLUS
DOCUMENT NUMBER: 148:85678
TITLE: Solid oral dosage form containing deacetylase inhibitor and an enhancer
INVENTOR(S): Leonard, Thomas W.; O'Toole, Edel; Feeney, Orlagh
PATENT ASSIGNEE(S): Merrion Research II Limited, Ire.
SOURCE: U.S. Pat. Appl. Publ., 38pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

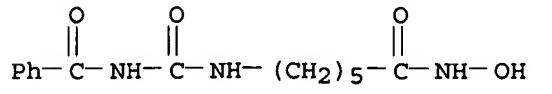
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007292512	A1	20071220	US 2007-761233	20070611
WO 2007146234	A2	20071221	WO 2007-US13693	20070611

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DQ, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-812523P P 20060609

AB The invention relates to a pharmaceutical composition, particularly oral dosage forms, comprising a DAC inhibitor in combination with an enhancer to promote absorption of the DAC inhibitor at the GIT cell lining. The enhancer is a medium chain fatty acid or derivative thereof having a carbon chain length of from 6 to 20 carbon atoms. In certain embodiments, the solid oral dosage form is a controlled release dosage form such as a delayed release dosage form. Thus, sustained release tablet was prepared containing sodium caprylate 65.7%, heparin 13.3%, silica dioxide 0.5%, magnesium stearate 0.5%, and mannitol 20.0%.

IT 851365-34-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid oral dosage form containing deacetylase inhibitor and an enhancer)
RN 851365-34-9 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl]amino]carbonyl]- (CA INDEX NAME)



L6 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:206787 HCAPLUS

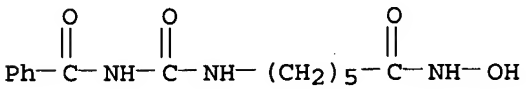
Updated Search

DOCUMENT NUMBER: 146:287512
TITLE: Development and validation of high-performance liquid chromatography-tandem mass spectrometry assay for 6-(3-benzoyl-ureido)-hexanoic acid hydroxyamide, a novel HDAC inhibitor, in mouse plasma for pharmacokinetic studies
AUTHOR(S): Yeo, Pauline; Xin, Liu; Goh, Evelyn; New, Lee Sun; Zeng, Peizi; Wu, Xiaofeng; Venkatesh, P.; Kantharaj, Ethirajulu
CORPORATE SOURCE: Department of Pharmacokinetics and Drug Metabolism, SBIO Pte Ltd, Singapore, 117528, Singapore
SOURCE: Biomedical Chromatography (2007), 21(2), 184-189
CODEN: BICHE2; ISSN: 0269-3879
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A liquid chromatog./tandem mass spectrometric method for the quantification of 6-(3-benzoyl-ureido)-hexanoic acid hydroxyamide (EX-2), a novel histone deacetylase (HDAC) inhibitor, in mouse plasma was developed to support inhouse pharmacokinetic (PK) studies in the lead optimization stage. In order to determine the PK parameters for EX-2 in comparison to other HDAC inhibitors such as Suberoylanilide hydroxamic acid (SAHA), PXD-101, and LBH-589, which are currently in different stages of clin. trials, research-grade bio-anal. method validations were carried out for EX-2 and these reference HDAC inhibitors, which were synthesized by inhouse medicinal chemists. The components of validation consisted of specificity, extraction efficiency, signal-response of calibration stds., lower limit of quantification, autosampler stability, and accuracy and precision of quality control samples. The validated LC/MS/MS methods were accurate and precise. The calibration curve ranged from 1 to 1600 ng/mL for all the analytes. The methods developed were used to quantify EX-2 and other HDAC inhibitors in mouse plasma obtained from pharmacokinetic studies. The results suggest that EX-2 has better PK parameters compared with the reference drugs and is a promising drug development candidate.

IT 851365-34-9, EX 2
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(development and validation of HPLC-tandem mass spectrometry assay for (benzoylureido)hexanoic acid hydroxyamide in mouse plasma for pharmacokinetic studies)

RN 851365-34-9 HCAPLUS
CN Benzamide, N-[[[6-(hydroxyamino)-6-oxohexyl]amino]carbonyl]- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:411563 HCAPLUS
DOCUMENT NUMBER: 140:391128
TITLE: Preparation of β-aminohydroxamic acids as peptide deformylase (PDF) inhibitors and their medical use
INVENTOR(S): Takayama, Wataru; Shirasaki, Masahisa; Inoue, Atsushi
PATENT ASSIGNEE(S): Senju Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.

Updated Search

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004143053	A	20040520	JP 2002-307534	20021022

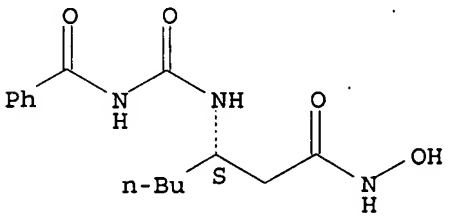
PRIORITY APPLN. INFO.: JP 2002-307534 20021022
OTHER SOURCE(S): MARPAT 140:391128

AB R2LG1NHCHR1CH2CONHOH [R1 = C1-5 linear or branched alkyl; R2 = (un)substituted aromatic hydrocarbyl, (un)substituted heterocyclyl; G1 = CO, SO2; L = G2NH, (CH2)n, CONR4CHR3, etc.; G2 = CO, SO2, bond; n = 0, 1; R3, R4 = H, C4-6 alkyl, R3R4 may be bonded to form C3-7 alkylene] or their salts, useful for inhibition of drug-resistant bacteria, are prepared Thus, amidation of (3S)-3-aminoheptanoic acid benzyloxyamide HCl salt with 2-naphthoyl chloride and hydrogenation of the product gave (1S)-naphthalene-2-carboxylic acid [1-(hydroxycarbamoylmethyl)pentyl]amide , which inhibited Ni-PDF from Escherichia coli with IC50 value of 4.656 μM.

IT 688002-83-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β-aminohydroxamic acids as peptide deformylase inhibitors and antibacterial agents)

RN 688002-83-7 HCAPLUS
CN Benzamide, N-[[[(1S)-1-[2-(hydroxyamino)-2-oxoethyl]pentyl]amino]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:491172 HCAPLUS
DOCUMENT NUMBER: 139:69520
TITLE: Preparation of N-sulfonyl amino acid hydroxamide derivatives as human ADAM-10 inhibitors
INVENTOR(S): Brown, S. David; Canne, Lynne; Co, Erick W.; Jammalamadaka, Vasu; Khoury, Richard G.; Kim, Moon Hwan; Le, Donna T.; Lew, Amy; Mac, Morrison B.; Mamo, Shumeye; Nuss, John M.; Prisbylla, Michael P.; Xu, Wei
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Updated Search

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003051825	A1	20030626	WO 2002-US39816		20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2473938	A1	20030626	CA 2002-2473938		20021213
AU 2002346724	A1	20030630	AU 2002-346724		20021213
EP 1461313	A1	20040929	EP 2002-784794		20021213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005513065	T	20050512	JP 2003-552713		20021213
US 2005227973	A1	20051013	US 2005-498338		20050511
PRIORITY APPLN. INFO.:			US 2001-340179P	P	20011214
			WO 2002-US39816	W	20021213

OTHER SOURCE(S): MARPAT 139:69520

AB The invention provides amino acid derivs. R5SO2NR4CHR3CONR2OR1 [R1 is H, alkyl, alkanoyl, (un)substituted arylalkyl or arylalkanoyl; R2 is any group given for R1 plus alkoxy; R3 is -Z-Q-J, where Z is (un)substituted alk(en)yl, alkoxyalkyl, or alkylthioalkyl; Q is a bond, CO, (un)substituted aryl, heteroaryl, or heterocycloalkyl; J is an amino group, including ureido groups; R4 is H, (un)substituted alkyl or arylalkyl; R5 is -M-G-A, where M and A are (un)substituted aryl or heteroaryl; G is a bond, CH2, -alkyl-O-, -O-alkyl-, O, S, SO, or SO2 (with provisos)] useful for inhibiting the ADAM-10 protein, also known as human Kuzbanian. Such compds. are useful in the in vitro study of the role of ADAM-10 (and its inhibition) in biol. processes. Pharmaceutical compns. comprising one or more ADAM-10 inhibitors are useful for the treatment of cancer, arthritis, and diseases related to angiogenesis. The invention also provides methods for making bis-aryl ether sulfonyl chloride intermediates. Thus, claimed compound N2-[[6-(3-fluorophenyl)pyridin-3-yl]sulfonyl]-N1-hydroxy-D-argininamide showed IC50 < 50 nM for inhibition of ADAM-10.

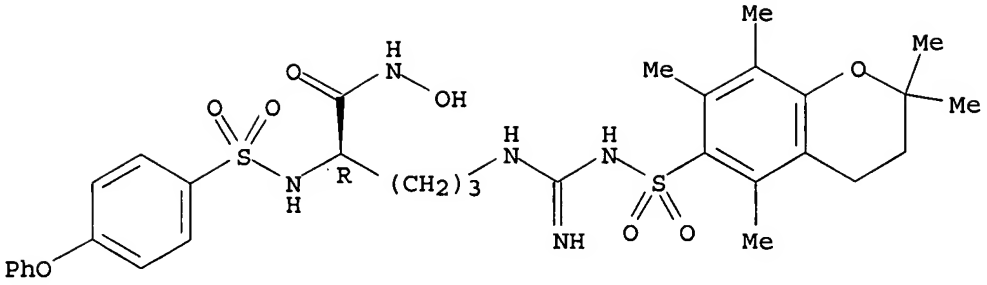
IT 549547-46-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-sulfonyl amino acid hydroxamide derivs. as human ADAM-10 inhibitors)

RN 549547-46-8 HCAPLUS

CN Pentanamide, 5-[[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]amino]-N-hydroxy-2-[[(4-phenoxyphenyl)sulfonyl]amino]-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.

Updated Search



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

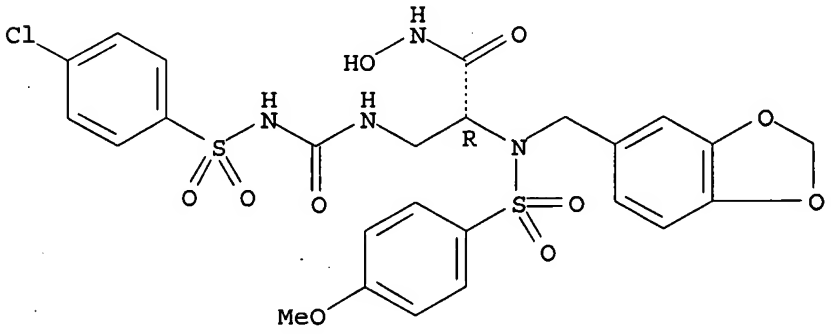
L6 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:442742 HCAPLUS
DOCUMENT NUMBER: 139:245665
TITLE: Novel Inhibitors of Procollagen C-Terminal Proteinase. Part 1: Diamino Acid Hydroxamates
AUTHOR(S): Delaet, N. G. J.; Robinson, L. A.; Wilson, D. M.; Sullivan, R. W.; Bradley, E. K.; Dankwardt, S. M.; Martin, R. L.; Van Wart, H. E.; Walker, K. A. M.
CORPORATE SOURCE: CombiChem Inc., San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(13), 2101-2104
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:245665

AB The parallel synthesis of novel inhibitors of procollagen C-terminal proteinase is described. The synthetic strategy allowed for the facile synthesis of a large number of side-chain diversified diamino acid hydroxamates, of which the d-diaminopropionic acid derivs. were shown to be single digit nanomolar PCP inhibitors.

IT 279255-40-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase synthesis and structure-activity relations of diamino acid hydroxamates as inhibitors of procollagen C-terminal proteinase)

RN 279255-40-2 HCAPLUS
CN Propanamide, 2-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-3-[[[[(4-chlorophenyl)sulfonyl]amino]carbonyl]amino]-N-hydroxy-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



Updated Search

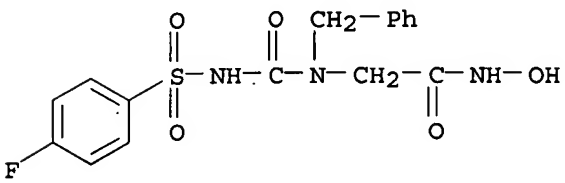
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:311217 HCAPLUS
DOCUMENT NUMBER: 139:245734
TITLE: Protease inhibitors: synthesis of bacterial collagenase and matrix metalloproteinase inhibitors incorporating arylsulfonylureido and 5-dibenzo-suberenyl/suberyl moieties
AUTHOR(S): Ilies, Monica; Banciu, Mircea D.; Scozzafava, Andrea; Ilies, Marc A.; Caproiu, Miron T.; Supuran, Claudiu T.
CORPORATE SOURCE: Polo Scientifico, Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Florence, 50019, Italy
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(10), 2227-2239
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:245734

AB Novel matrix metalloproteinase (MMP)/bacterial collagenase inhibitors are reported, considering the sulfonylated amino acid hydroxamates as lead mols. A series of compds. was prepared by reaction of arylsulfonyl isocyanates with N-(5H-dibenzo[a,d]cycloheptен-5-yl)- and N-(10,11-dihydro-5H-dibenzo[a,d]cycloheptен-5-yl) Me glycocolate, resp., followed by the conversion of the COOMe to the carboxylate/hydroxamate moieties. The corresponding derivs. with methylene and ethylene spacers between the polycyclic moiety and the amino acid functionality were also obtained by related synthetic strategies. These new compds. were assayed as inhibitors of MMP-1, MMP-2, MMP-8 and MMP-9, and of the collagenase isolated from Clostridium histolyticum (ChC). Some of the new derivs. reported here proved to be powerful inhibitors of the four MMPs mentioned above and of ChC, with activities in the low nanomolar range for some of the target enzymes, depending on the substitution pattern at the sulfonylureido moiety and on the length of the spacer through which the dibenzosuberenyl/suberyl group is connected with the rest of the mol. Several of these inhibitors also showed selectivity for the deep pocket enzymes (MMP-2, MMP-8 and MMP-9) over the shallow pocket ones MMP-1 and ChC.

IT 276695-94-4
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation of arylsulfonylureido- and dibenzosuberenyl/suberyl-containing compds. as matrix metalloproteinase/bacterial collagenase inhibitors)

RN 276695-94-4 HCAPLUS
CN Acetamide, 2-[[[[(4-fluorophenyl)sulfonyl]amino]carbonyl](phenylmethyl)amino]-N-hydroxy- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Updated Search

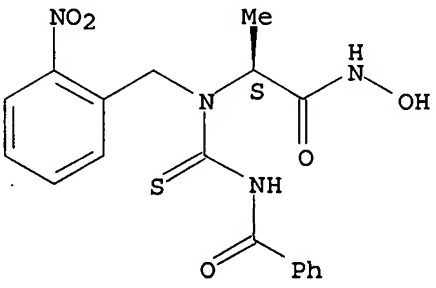
L6 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:381037 HCAPLUS
DOCUMENT NUMBER: 135:133815
TITLE: Protease Inhibitors: Synthesis of a Series of Bacterial Collagenase Inhibitors of the Sulfonyl Amino Acyl Hydroxamate Type
AUTHOR(S): Clare, Brian W.; Scozzafava, Andrea; Supuran, Claudiu T.
CORPORATE SOURCE: Department of Chemistry, The University of Western Australia, 6009, Australia
SOURCE: Journal of Medicinal Chemistry (2001), 44(13), 2253-2258
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:133815

AB A series of sulfonyl amino acyl hydroxamates incorporating alkyl/arylsulfonyl-N-2-nitrobenzyl-L-alanine was prepared Related compds. were obtained by reaction of N-2-nitrobenzyl-L-Ala with aryl isocyanates, arylsulfonyl isocyanates, or benzoyl isothiocyanate, followed by the conversion of the COOH into the CONHOH moiety. The new compds. were assayed as inhibitors of the Clostridium histolyticum collagenase (ChC), a bacterial protease involved in the degradation of extracellular matrix. Many of the obtained hydroxamates proved to be effective bacterial collagenase inhibitors, the main contributor to activity being the substitution pattern at the sulfonamido moiety. The best ChC inhibitors were those containing pentafluorophenylsulfonyl and 3- and 4-protected-aminophenylsulfonyl P1' groups among others, with affinities in the low nanomolar range. This study also proves that the 2-nitrobenzyl- moiety, similarly to the 4-nitrobenyl one previously investigated is an efficient P2' anchoring moiety for obtaining potent bacterial collagenase inhibitors.

IT 351527-61-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of a series of bacterial collagenase inhibitors of the sulfonyl amino acyl hydroxamate type)

RN 351527-61-2 HCAPLUS
CN Benzamide, N-[[[(1S)-2-(hydroxyamino)-1-methyl-2-oxoethyl][(2-nitrophenyl)methyl]amino]thioxomethyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN

Updated Search

ACCESSION NUMBER: 2001:314178 HCAPLUS
DOCUMENT NUMBER: 134:326767
TITLE: Preparation of acetylenic α-amino acid-based sulfonamide hydroxamic acid TACE inhibitors
INVENTOR(S): Levin, Jeremy I.; Chen, James M.; Cole, Derek C.; Du, Mila T.; Laakso, Leif M.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: U.S., 109 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6225311	B1	20010501	US 2000-492691	20000127
US 2003008849	A1	20030109	US 2000-748912	20001227
US 2003212049	A1	20031113	US 2003-376871	20030227
US 6716833	B2	20040406		
US 2004033988	A1	20040219	US 2003-377008	20030227
US 6812227	B2	20041102		
US 2005113346	A1	20050526	US 2004-977962	20041029

PRIORITY APPLN. INFO.:
US 1999-155249P P 19990127
US 2000-492691 A3 20000127
US 2000-748912 B1 20001227
US 2003-377008 A1 20030227

OTHER SOURCE(S): MARPAT 134:326767

AB Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO2, P(O)R10, where R10 = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R1 = H, aryl, alkyl, alkenyl, alkynyl; R2 = any group given for R1, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R1 and R2 may form a ring; R3 = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R1 and R3 may form a ring; R4, R5 = H, alkyl, CN, C.tplbond.CH; R6 = any group given for R1, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepared as inhibitors of TNF-α converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-methylbutyramide was prepared and showed IC50 = 7.4 nM for inhibition of TACE.

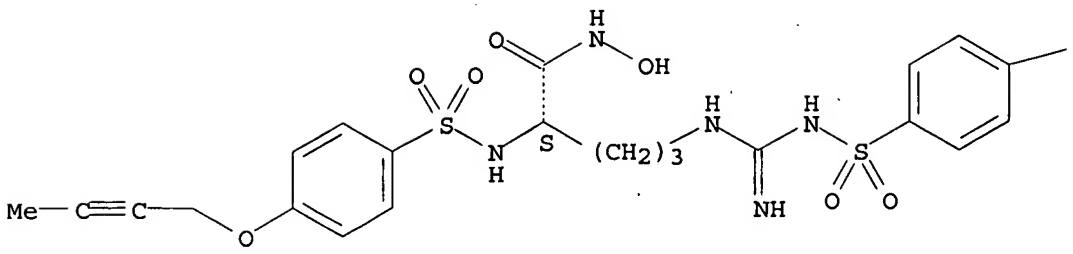
IT 287403-59-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acetylenic α-amino acid-based sulfonamide hydroxamic acid TACE inhibitors)

RN 287403-59-2 HCAPLUS
CN Pentanamide, 2-[[[4-(2-butynyloxy)phenyl]sulfonyl]amino]-N-hydroxy-5-[[imino[[(4-methylphenyl)sulfonyl]amino]methyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Updated Search

PAGE 1-A



PAGE 1-B

Me

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:535102 HCAPLUS
DOCUMENT NUMBER: 133:150908
TITLE: Preparation of acetylenic α-amino acid-based sulfonamide hydroxamic acid TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Chen, James Ming; Cole, Derek Cecil
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044709	A2	20000803	WO 2000-US1981	20000127
WO 2000044709	A3	20001221		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356299	A1	20000803	CA 2000-2356299	20000127
EP 1144368	A2	20011017	EP 2000-905750	20000127
EP 1144368	B1	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000007752	A	20011204	BR 2000-7752	20000127
TR 200102132	T2	20020121	TR 2001-2132	20000127
JP 2002535382	T	20021022	JP 2000-595966	20000127
AU 766717	B2	20031023	AU 2000-27384	20000127
NZ 511928	A	20031128	NZ 2000-511928	20000127
TW 593247	B	20040621	TW 2000-89101287	20000127
AT 271035	T	20040715	AT 2000-905750	20000127
PT 1144368	T	20040930	PT 2000-905750	20000127
CN 1550496	A	20041201	CN 2004-10032424	20000127

Updated Search

HU 2004002263	A2	20050228	HU 2004-2263		20000127
HU 2004002263	A3	20060529			
ES 2225089	T3	20050316	ES 2000-905750		20000127
ZA 2001004326	A	20020826	ZA 2001-4326		20010525
NO 2001003674	A	20010924	NO 2001-3674		20010726
MX 2001PA07579	A	20011203	MX 2001-PA7579		20010726
BG 105738	A	20020531	BG 2001-105738		20010726
IN 2001KN00867	A	20051216	IN 2001-KN867		20010823
HK 1038735	A1	20050107	HK 2002-100184		20020110
PRIORITY APPLN. INFO.:			US 1999-238255	A	19990127
			WO 2000-US1981	W	20000127
			IN 2001-538	A3	20010522

OTHER SOURCE(S): MARPAT 133:150908

AB Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO2, P(O)R10, where R10 = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH2, S; R1 = H, aryl, alkyl, alkenyl, alkynyl; R2 = any group given for R1, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R1 and R2 may form a ring; R3 = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R1 and R3 may form a ring; R4, R5 = H, alkyl, CN, C.tplbond.CH; R6 = any group given for R1, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepared as inhibitors of TNF-α converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-methylbutyramide was prepared and showed IC50 = 7.4 nM for inhibition of TACE.

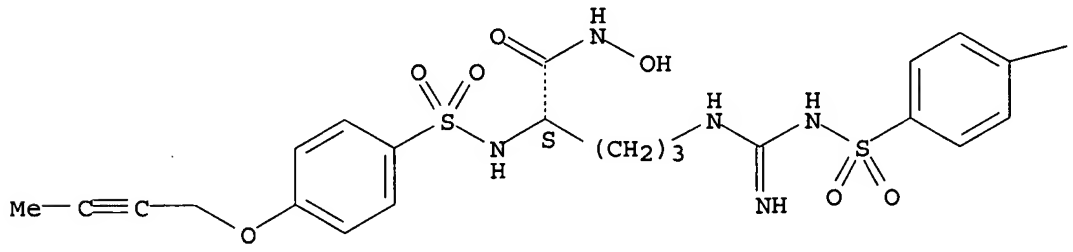
IT 287403-59-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acetylenic α-amino acid-based sulfonamide hydroxamic acid TACE inhibitors)

RN 287403-59-2 HCAPLUS

CN Pentanamide, 2-[[[4-(2-butynyloxy)phenyl]sulfonyl]amino]-N-hydroxy-5-[[imino[[(4-methylphenyl)sulfonyl]amino]methyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—Me

L6 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:453771 HCAPLUS
DOCUMENT NUMBER: 133:234316

Updated Search

TITLE: Protease inhibitors. Part 12. Synthesis of potent matrix metalloproteinase and bacterial collagenase inhibitors incorporating sulfonylated N-4-nitrobenzyl-β-alanine hydroxamate moieties

AUTHOR(S): Scozzafava, A.; Ilies, M. A.; Manole, G.; Supuran, C. T.

CORPORATE SOURCE: Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, I-50121, Italy

SOURCE: European Journal of Pharmaceutical Sciences (2000), 11(1), 69-79
CODEN: EPSCED; ISSN: 0928-0987

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

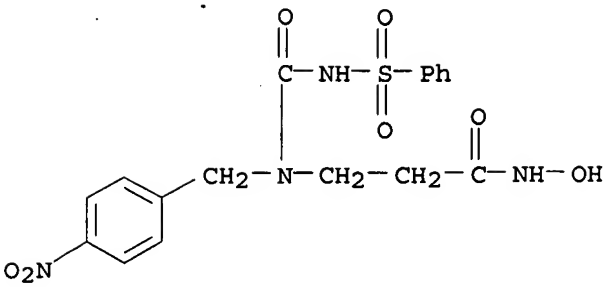
AB N-4-Nitrobenzyl-β-alanine was reacted with alkyl/arylsulfonyl halides, followed by conversion of the COOH to the CONHOH group. Structurally related compds. were obtained by reaction of N-4-nitrobenzyl-β-alanine with aryl isocyanates, arylsulfonyl isocyanates or benzoyl isothiocyanate, followed by similar conversion of the COOH into the CONHOH moiety. Another subseries of derivs. was prepared from sulfanilyl- or metanilyl-4-nitrobenzyl-β-alanine by reaction with arylsulfonyl isocyanates, followed by the introduction of the hydroxamate moiety. The new compds. were assayed as inhibitors of four matrix metalloproteinases (MMPs), MMP-1, MMP-2, MMP-8 and MMP-9, and of the Clostridium histolyticum collagenase (ChC). Some of the prepared hydroxamate derivs. proved to be very effective collagenase/gelatinase inhibitors, depending on the substitution pattern at the sulfonamido moiety. Substitutions leading to the best inhibitors of MMP-1, a short-pocket enzyme, were those involving pentafluorophenylsulfonyl or 3-trifluoromethyl-phenylsulfonyl at P1' (KI of 3-5 nM). For MMP-2, MMP-8 and MMP-9 (deep-pocket enzymes), the best inhibitors were those containing perfluoroalkylsulfonyl- and substituted-arylsulfonyl moieties, such as pentafluorophenylsulfonyl, 3- and 4-protected-aminophenylsulfonyl-, 3- and 4-carboxy-phenylsulfonyl-, arylsulfonylureido- or arylsulfonylureido-sulfanilyl-/metanilyl moieties at P1'. Bulkier groups in this position, such as 1- and 2-naphthyl-, substituted-naphthyl or quinoline-8-yl-moieties, among others, led to less effective MMP/ChC inhibitors. The best ChC inhibitors were again those containing pentafluorophenylsulfonyl, 3- and 4-protected-aminophenylsulfonyl P1' groups. This study demonstrates that the 4-nitrobenzyl moiety, investigated here for the first time, is an efficient P2' anchoring moiety, whereas the β-alanyl scaffold can successfully replace the α-amino acyl one, for obtaining potent MMP/ChC inhibitors.

IT 294200-67-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of potent matrix metalloproteinase and bacterial collagenase inhibitors incorporating sulfonylated nitrobenzylalanine hydroxamate moieties)

RN 294200-67-2 HCAPLUS

CN Propanamide, N-hydroxy-3-[[(4-nitrophenyl)methyl][[(phenylsulfonyl)amino]carbonyl]amino]- (CA INDEX NAME)

Updated Search



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:441768 HCAPLUS
DOCUMENT NUMBER: 133:74324
TITLE: Preparation of amino acid sulfonamide hydroxamates as inhibitors of procollagen C-proteinase.
INVENTOR(S): Billedeau, Roland Joseph; Broka, Chris Allen; Campbell, Jeffrey Allen; Chen, Jian Jeffrey; Dankwardt, Sharon Marie; Delaet, Nancy; Robinson, Leslie Ann; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037436	A1	20000629	WO 1999-EP9920	19991214
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2355902	A1	20000629	CA 1999-2355902	19991214
BR 9916504	A	20010911	BR 1999-16504	19991214
EP 1149072	A1	20011031	EP 1999-963530	19991214
EP 1149072	B1	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101868	T2	20011121	TR 2001-1868	19991214
HU 2001004658	A2	20020629	HU 2001-4658	19991214
HU 2001004658	A3	20051228		
JP 2002533322	T	20021008	JP 2000-589508	19991214
AU 769319	B2	20040122	AU 2000-19792	19991214
NZ 512292	A	20040326	NZ 1999-512292	19991214
AT 270271	T	20040715	AT 1999-963530	19991214
RU 2232751	C2	20040720	RU 2001-119461	19991214
US 6492394	B1	20021210	US 1999-469660	19991222
HR 2001000443	A1	20020630	HR 2001-443	20010614
ZA 2001005014	A	20020919	ZA 2001-5014	20010619
MX 2001PA06328	A	20010910	MX 2001-PA6328	20010620

Updated Search

IN 2001CN00859	A	20050304	IN 2001-CN859		20010620
NO 2001003100	A	20010821	NO 2001-3100		20010621
US 2003199520	A1	20031023	US 2002-267292		20021009
US 6844366	B2	20050118			
US 2003216405	A1	20031120	US 2002-267727		20021009
US 6787559	B2	20040907			
PRIORITY APPLN. INFO.:			US 1998-113311P	P	19981222
			US 1999-147053P	P	19990803
			US 1999-164138P	P	19991108
			WO 1999-EP9920	W	19991214
			US 1999-469660	A3	19991222

OTHER SOURCE(S): MARPAT 133:74324

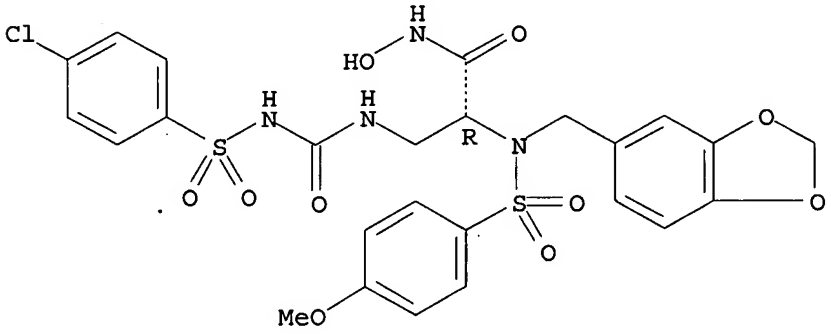
AB HOHNCOCHR1NRSO2Ar2 [R1 = alkyl, haloalkyl, heteroalkyl, cycloalkyl, aryl, aralkyl, aralkenyl, heteroaryl, heteroaralkyl, aminl, aryl, aralkyl, etc.; R = CHR2Ar1, CHR2CH:CHAr1; Ar2 = specified (substituted) Ph, naphthyl; R2 = H, alkyl; with provisos], were prepared Thus, N-hydroxy-2(R)-[(3,4-methylenedioxybenzyl)(4-methoxy-2,3,6-trimethylbenzenesulfonyl)amino]-3-methylbutyramide was prepared by solution phase synthesis from BOC-D-Val-OH. Title compds. inhibited procollagen C-proteinase with IC50 0.01-2 μM.

IT 279255-40-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid sulfonamide hydroxamates as inhibitors of procollagen C-proteinase)

RN 279255-40-2 HCAPLUS

CN Propanamide, 2-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-3-[[[[(4-chlorophenyl)sulfonyl]amino]carbonyl]amino]-N-hydroxy-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2000:401856 HCAPLUS
DOCUMENT NUMBER:	133:43814
TITLE:	Preparation of peptides as procollagen C-proteinase inhibitors
INVENTOR(S):	Dankwardt, Sharon Marie; Van Wart, Harold Edgar; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S):	F. Hoffmann-La Roche A.-G., Switz.
SOURCE:	PCT Int. Appl., 78 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

Updated Search

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000034313	A1	20000615	WO 1999-EP9519	19991206
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2352740	A1	20000615	CA 1999-2352740	19991206
BR 9916004	A	20011002	BR 1999-16004	19991206
EP 1137661	A1	20011004	EP 1999-968338	19991206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101663	T2	20011121	TR 2001-1663	19991206
JP 2002531576	T	20020924	JP 2000-586755	19991206
AU 772575	B2	20040429	AU 2000-25375	19991206
US 6426402	B1	20020730	US 1999-459201	19991210
MX 2001PA05750	A	20011001	MX 2001-PA5750	20010607
ZA 2001004672	A	20020909	ZA 2001-4672	20010607
US 2002169133	A1	20021114	US 2002-72730	20020207
US 6951918	B2	20051004		

PRIORITY APPLN. INFO.:	US 1998-111661P	P	19981210
	WO 1999-EP9519	W	19991206
	US 1999-459201	A3	19991210

OTHER SOURCE(S): MARPAT 133:43814

AB Peptides R7-Z-An-NR6CR4R5CONR3CR1R2CONHOH [R1, R3, R4 = H, alkyl; R2 = cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heterocyclyl, heterocycloalkyl, or -(alkylene)-B-X, where B = O, NR8 (R8 = H, alkyl), S, SO, SO2, CO, CONR8, NR8CO2, NR8SO2, C(:NR8)NR8SO2, NR8CO and X = cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl or R2 and R3 form an alkylene or heteroalkylene chain; R6 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl; R5 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heterocycloalkyl, heteroalkyl, or -(alkylene)-CO-X1, where X1 = alkyl, OH, alkoxy, aryl, aralkyl, aryloxy, aralkyloxy, heteroaryl, heteroaryloxy, heteroaralkyloxy, or amino group or R5 and R4 or R5 and R6 form an alkylene group; n = 0 or 1; A = COCHR9(CH2)mNR10, where m = 0-5, R9 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or -(alkylene)-CO-X1 and R10 = H, alkyl, aralkyl, or heteroaralkyl; Z = Y-B, where Y = alkylene or a bond and B = CO, CO2, CONR8, SO2, SO2NR8, (un)substituted alkylene, or a bond; R7 = cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl, provided that when n = 0 and Z = SO2, R2 does not contain an imidazole group] were prepared as procollagen C-proteinase inhibitors. General exptl. procedures are given for solid-phase synthesis of the claimed peptides. Compds. such as (S,S)-CbzNHCHPhCONHCH(CH2-T)CONHOH (T = 4-thiazolyl, Cbz = benzyloxycarbonyl) showed IC50 in the range 0.02 to 200 μM for inhibition procollagen C-proteinase.

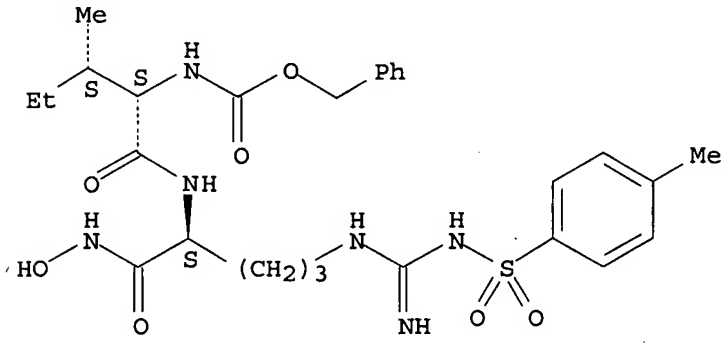
IT 274936-38-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as procollagen C-proteinase inhibitors)

RN 274936-38-8 HCAPLUS

Updated Search

CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-N-hydroxy-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:368315 HCAPLUS
DOCUMENT NUMBER: 133:177439
TITLE: Protease inhibitors: synthesis of L-alanine hydroxamate sulfonylated derivatives as inhibitors of Clostridium histolyticum collagenase
AUTHOR(S): Supuran, Claudiu T.; Briganti, Fabrizio; Mincione, Giovanna; Scozzafava, Andrea
CORPORATE SOURCE: Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, I-50121, Italy
SOURCE: Journal of Enzyme Inhibition (2000), 15(2), 111-128
CODEN: ENINEG; ISSN: 8755-5093
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB L-alanine hydroxamate derivs. were obtained by reaction of alkyl/arylsulfonyl halides with L-alanine, followed by treatment with benzyl chloride, and conversion of the COOH moiety to the CONHOH group with hydroxylamine in the presence of carbodiimides. Other derivs. were obtained by reaction of N-benzyl-alanine with aryl isocyanates, arylsulfonyl isocyanates or benzoyl isothiocyanate, followed by a similar conversion of the COOH to the CONHOH moiety. The obtained compds. were assayed as inhibitors of Clostridium histolyticum collagenase, ChC (EC 3.4.24.3), a zinc enzyme which degrades triple helical collagen. The hydroxamate derivs. were generally 100-500 times more active than the corresponding carboxylates. In the series of synthesized derivs., substitution patterns leading to the most potent ChC inhibitors were those involving perfluoroalkylsulfonyl- and substituted-arylsulfonyl moieties, such as pentafluorophenylsulfonyl, 3- and 4-protected-aminophenylsulfonyl-, 3- and 4-carboxyphenylsulfonyl-, 3-trifluoromethyl-phenylsulfonyl-, or 1- and 2-naphthylsulfonyl among others. Similarly to the matrix metalloproteinase (MMP) hydroxamate inhibitors, ChC inhibitors of the type reported here must incorporate hydrophobic moieties at the P2' and P3' sites, in order to achieve tight binding to the enzyme.

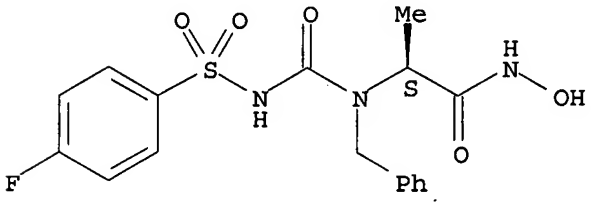
IT 288266-28-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of L-alanine hydroxamate sulfonylated derivs. as inhibitors of

Clostridium histolyticum collagenase)

RN 288266-28-4 HCAPLUS

CN Propanamide, 2-[[[[(4-fluorophenyl)sulfonyl]amino]carbonyl](phenylmethyl)amino]-N-hydroxy-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:261412 HCAPLUS

DOCUMENT NUMBER: 133:53160

TITLE: Protease inhibitors - part 5. Alkyl/arylsulfonyl- and arylsulfonylureido-/arylureido- glycine hydroxamate inhibitors of Clostridium histolyticum collagenase

AUTHOR(S): Scozzafava, Andrea; Supuran, Claudiu T.

CORPORATE SOURCE: Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Florence, I-50121, Italy

SOURCE: European Journal of Medicinal Chemistry (2000), 35(3), 299-307
CODEN: EJMCA5; ISSN: 0223-5234

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Reaction of alkyl/arylsulfonyl halides with glycine afforded a series of derivs. which were first N-benzylated by treatment with benzyl chloride, and then converted to the corresponding hydroxamic acids with hydroxylamine in the presence of carbodiimide derivs. Other derivs. were obtained by reaction of N-benzyl-glycine with aryl isocyanates, arylsulfonyl isocyanates or benzoyl isothiocyanate, followed by conversion of their COOH group into the CONHOH moiety, as mentioned above. The 90 new compds. reported here were assayed as inhibitors of the Clostridium histolyticum collagenase (EC 3.4.24.3), a zinc enzyme which degrades triple helical regions of native collagen. The prepared hydroxamate derivs. were generally 100-500 times more active than the corresponding carboxylates. In the series of synthesized hydroxamates, substitution patterns leading to the best inhibitors were those involving perfluoroalkylsulfonyl- and substituted-arylsulfonyl moieties, such as pentafluorophenylsulfonyl, 3- and 4-carboxyphenylsulfonyl-, 3-trifluoromethyl-phenylsulfonyl or 1- and 2-naphthyl among others. Thus, it seems that similarly to the matrix metalloproteinase (MMP) hydroxamate inhibitors, Clostridium histolyticum collagenase inhibitors should incorporate hydrophobic moieties at the P1' and P2' sites, whereas the α-carbon substituent may be a small and compact moiety (such as H, for the Gly derivs. reported here). Such compds. might lead to the design of collagenase inhibitor-based drugs useful as anti-cancer, anti-arthritis or anti-bacterial agents for the treatment of corneal keratitis.

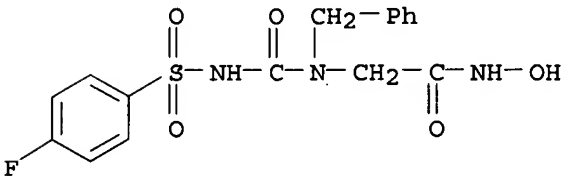
IT 276695-94-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

Updated Search

(alkyl/arylsulfonyl- and arylsulfonylureido-/arylureido- glycine hydroxamate inhibitors of Clostridium histolyticum collagenase)

RN 276695-94-4 HCAPLUS

CN Acetamide, 2-[[[[(4-fluorophenyl)sulfonyl]amino]carbonyl](phenylmethyl)amino]-N-hydroxy- (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:222313 HCAPLUS

DOCUMENT NUMBER: 133:26475

TITLE: Protease Inhibitors: Synthesis of Potent Bacterial Collagenase and Matrix Metalloproteinase Inhibitors Incorporating N-4-Nitrobenzylsulfonylglycine Hydroxamate Moieties

AUTHOR(S): Scozzafava, Andrea; Supuran, Claudiu T.

CORPORATE SOURCE: Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Florence, I-50121, Italy

SOURCE: Journal of Medicinal Chemistry (2000), 43(9), 1858-1865
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

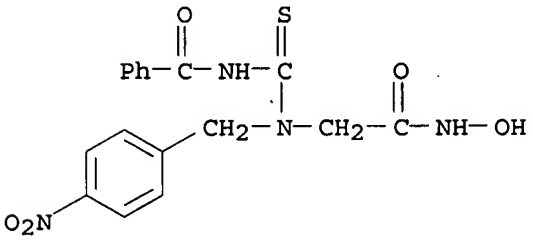
LANGUAGE: English

AB A series of compds. was prepared by reaction of alkyl/arylsulfonyl halides with N-4-nitrobenzylglycine, followed by conversion of the COOH to the CONHOH group, with hydroxylamine in the presence of carbodiimides. Other structurally related compds. were obtained by reaction of N-4-nitrobenzylglycine with aryl isocyanates, arylsulfonyl isocyanates, or benzoyl isothiocyanate, followed by the similar conversion of the COOH into the CONHOH moiety. Another subseries of derivs. was prepared from sulfanilyl- or metanilyl-4-nitrobenzylglycine by reaction with arylsulfonyl isocyanates, followed by conversion of the COOH to the hydroxamate moiety. The new compds. were assayed as inhibitors of four matrix metalloproteinases (MMPs), MMP-1, MMP-2, MMP-8, and MMP-9, and of the Clostridium histolyticum collagenase (ChC). Some of the prepared hydroxamate derivs. proved to be very effective collagenase/gelatinase inhibitors, depending on the substitution pattern at the sulfonamido moiety. Substitutions leading to best inhibitors of MMP-1, a short pocket enzyme, were those involving pentafluorophenylsulfonyl or 3-trifluoromethylphenylsulfonyl moieties at P1' (KI's of 3-5 nM). For MMP-2, MMP-8, and MMP-9 (deep-pocket enzymes), best inhibitors were especially those containing long perfluoroalkylsulfonyl and substituted-arylsulfonyl moieties, such as pentafluorophenylsulfonyl, 3- and 4-protected-aminophenylsulfonyl, 3- and 4-carboxyphenylsulfonyl, arylsulfonylureido, or arylsulfonylureidosulfanilyl/metanilyl moieties, at P1'. Bulkier groups in this position, such as 1- and 2-naphthyl, substituted-naphthyl, or quinolin-8-yl moieties among others, led to less effective MMP/ChC inhibitors. Best ChC inhibitors were again those containing pentafluorophenylsulfonyl or 3- and 4-protected-aminophenylsulfonyl P1' anchoring groups, suggesting that this protease is also a short-pocket

wider-neck one (more similar to MMP-1). This study also proves that the 4-nitrobenzyl moiety is an efficient P2' anchoring moiety and that sulfonylureido, ureido, or carboxythioureido substitutions at P1' are also tolerated for obtaining potent sulfonylated amino acid hydroxamate-like MMP/ChC inhibitors.

IT 273732-17-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of potent bacterial collagenase and matrix metalloproteinase inhibitors incorporating nitrobenzylsulfonylglycine hydroxamate moieties)

RN 273732-17-5 HCAPLUS
CN Benzamide, N-[[[2-(hydroxyamino)-2-oxoethyl][(4-nitrophenyl)methyl]amino]thioxomethyl]- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

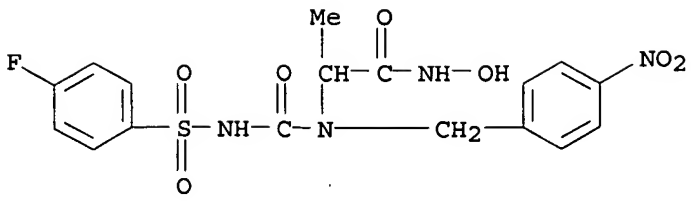
L6 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:208763 HCAPLUS
DOCUMENT NUMBER: 132:305057
TITLE: Protease inhibitors: synthesis of Clostridium histolyticum collagenase inhibitors incorporating sulfonyl-L-alanine hydroxamate moieties
AUTHOR(S): Scozzafava, Andrea; Supuran, Claudiu T.
CORPORATE SOURCE: Universita degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Florence, 50121, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(5), 499-502
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of hydroxamates was obtained by the reaction of N-(4-nitrobenzyl)-L-alanine with alkyl/arylsulfonyl halides, followed by conversion of the CO2H group into CONHOH (no data). Structurally related compds. were prepared similarly by using arylsulfonyl isocyanates, aryl isocyanates or arylsulfenyl halides instead of the sulfonyl halides (no data). Many of the new compds. showed nanomolar affinity for the bacterial collagenase isolated from the pathogen Clostridium histolyticum.

IT 265668-34-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Clostridium collagenase inhibitors incorporating sulfonylalanine hydroxamate)

RN 265668-34-6 HCAPLUS
CN Propanamide, 2-[[[[(4-fluorophenyl)sulfonyl]amino]carbonyl][(4-nitrophenyl)methyl]amino]-N-hydroxy- (CA INDEX NAME)

Updated Search



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:157028 HCAPLUS
DOCUMENT NUMBER: 132:344757
TITLE: Protease inhibitors. Part 8. Synthesis of potent Clostridium histolyticum collagenase inhibitors incorporating sulfonylated L-alanine hydroxamate moieties
AUTHOR(S): Scozzafava, A.; Supuran, C. T.
CORPORATE SOURCE: Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Florence, I-50121, Italy
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(3), 637-645
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

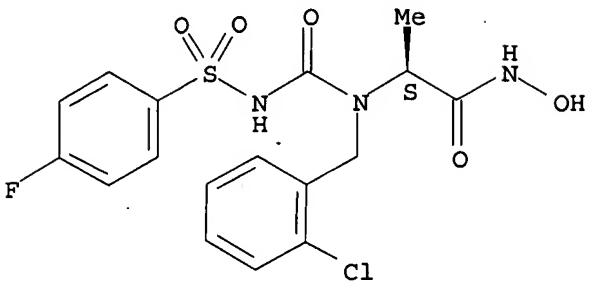
AB A series of hydroxamates was prepared by reaction of alkyl/arylsulfonyl halides with N-2-chlorobenzyl-L-alanine, followed by conversion of the CO2H moiety to the CONHOH group, with NH2OH in the presence of carbodiimides. Other structurally related compds. were obtained by reaction of N-2-chlorobenzyl-L-alanine with aryl isocyanates, arylsulfonyl isocyanates, or benzoyl isothiocyanate, followed by the similar conversion of the CO2H into the CONHOH moiety. The new compds. were assayed as inhibitors of the Clostridium histolyticum collagenase, ChC (EC 3.4.24.3), a bacterial Zn metallo-peptidase which degrades triple helical collagen as well as a large number of synthetic peptides. The prepared hydroxamates proved to be 100-500+ more active collagenase inhibitors than the corresponding carboxylates. Substitution patterns leading to best ChC inhibitors (both for carboxylates as well as for the hydroxamates) were those involving perfluoroalkylsulfonyl- and substituted arylsulfonyl moieties, such as C6F5SO2, protected 3- and 4-aminophenylsulfonyl-, 3-/4-HO2CC6H4SO2, 3-F3CC6H4SO2, as well as 1- and 2-naphthyl-, quinolin-8-yl- or substituted-arylsulfonylamido-carboxyl moieties among others. Similarly to the matrix metalloproteinase (MMP) hydroxamate inhibitors, ChC inhibitors of the type reported here must incorporate hydrophobic moieties at the P2' and P3' sites, to achieve tight binding to the enzyme. This study also proves that the 2-chlorobenzyl moiety, is an efficient P2' anchoring moiety for obtaining potent ChC inhibitors.

IT 269747-00-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of Clostridium collagenase inhibitors incorporating sulfonylated alanine hydroxamate)

RN 269747-00-4 HCAPLUS
CN Propanamide, 2-[[(2-chlorophenyl)methyl][[[(4-fluorophenyl)sulfonyl]amino]carbonyl]amino]-N-hydroxy-, (2S)- (CA INDEX NAME)

Updated Search

Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:142412 HCAPLUS
DOCUMENT NUMBER: 132:342787
TITLE: Protease inhibitors. Part 7 Inhibition of Clostridium histolyticum collagenase with sulfonylated derivatives of l-valine hydroxamate
AUTHOR(S): Supuran, C. T.; Scozzafava, A.
CORPORATE SOURCE: Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Florence, I-50121, Italy
SOURCE: European Journal of Pharmaceutical Sciences (2000), 10(1), 67-76
CODEN: EPSCED; ISSN: 0928-0987
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

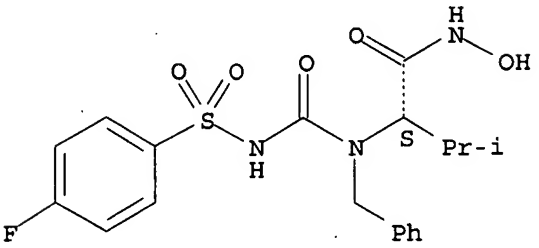
AB Sulfonylated l-valine hydroxamate derivs. were obtained by reaction of alkyl/arylsulfonyl halides with the title amino acid, followed by treatment with benzyl chloride, and conversion of the COOH moiety to the CONHOH group. Other derivs. were obtained by reaction of N-benzyl-l-valine with arylisocyanates, arylsulfonylisocyanates or benzoylisothiocyanate, followed by the similar conversion of the COOH into the CONHOH moiety, with hydroxylamine in the presence of carbodiimides. The obtained compds. were assayed as inhibitors of the Clostridium histolyticum collagenase, ChC (EC 3.4.24.3), a zinc enzyme which degrades triple helical collagen. The hydroxamate derivs. were generally 100-500 times more active than the corresponding carboxylates. In the series of synthesized derivs., substitution patterns leading to best ChC inhibitors were those involving perfluoroalkylsulfonyl- and substituted-arylsulfonyl moieties, such as pentafluorophenylsulfonyl; 3- and 4-protected-aminophenylsulfonyl-; 3- and 4-carboxyphenylsulfonyl-; 3-trifluoromethylphenylsulfonyl; or 1- and 2-naphthyl among others. Similarly to the matrix metalloproteinase hydroxamate inhibitors, ChC inhibitors of the type reported here must incorporate hydrophobic moieties at the P2' and P3' subsites, in order to achieve tight binding to the enzyme. Such compds. might lead to drugs useful in the treatment of corneal bacterial keratitis.

IT 270072-80-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonylated valine hydroxamates as inhibitors of Clostridium histolyticum collagenase)
RN 270072-80-5 HCAPLUS
CN Butanamide, 2-[[[[(4-fluorophenyl)sulfonyl]amino]carbonyl](phenylmethyl)am

Updated Search

ino]-N-hydroxy-3-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

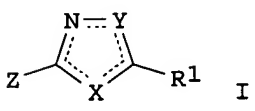


REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:691089 HCAPLUS
DOCUMENT NUMBER: 131:310839
TITLE: Preparation of heterocyclyl peptide derivatives as cysteine protease inhibitors
INVENTOR(S): Spruce, Lyle W.; Gyorkos, Albert C.; Cheronis, John C.; Goodfellow, Val S.; Leimer, Axel H.; Young, John M.; Gerrity, James I.
PATENT ASSIGNEE(S): Cortech Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9954317	A1	19991028	WO 1999-US8501		19990423
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6004933	A	19991221	US 1998-65258		19980423
CA 2329712	A1	19991028	CA 1999-2329712		19990423
AU 9939651	A	19991108	AU 1999-39651		19990423
AU 750369	B2	20020718			
NZ 507696	A	20031031	NZ 1999-507696		19990423
MX 2000PA10379	A	20010430	MX 2000-PA10379		20001023
PRIORITY APPLN. INFO.:			US 1998-65258	A	19980423
			WO 1999-US8501	W	19990423

OTHER SOURCE(S): MARPAT 131:310839
GI



I

Updated Search

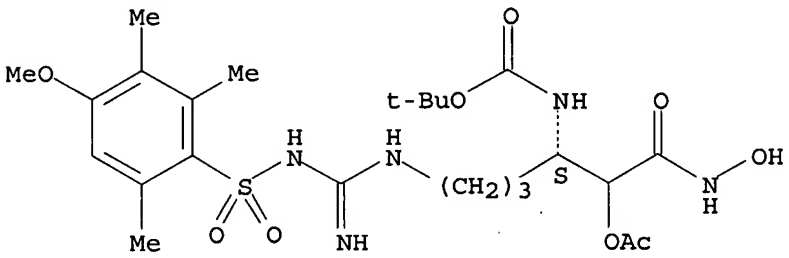
AB Compds. I (Z is a cysteine protease binding moiety; R1 = alkyl or alkenyl optionally substituted by halo or hydroxy, alkylamino, dialkylamino, alkyldialkylamino, or cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, aryl, arylalkyl, or arylalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted by halo, cyano, nitro, amino, alkyl, aryl, etc.; Y, X = O, S, or optionally substituted N) were prepared as cysteine protease inhibitors. Thus, N-[1(S)-[[5-(3-methylbenzyl)-1,3,4-oxadiazol-2-yl]carbonyl]-2-methylpropyl]-L-phenylalaninamide-(3R)-(isobutyl)succinic acid, prepared from 3(S)-[(benzyloxycarbonyl)amino]-2-acetoxy-4-methylpentanenitrile, 3-methylphenylacetic hydrazide, 4-methylvaleric acid, (S)-(-)-4-benzyl-2-oxazolidinone, tert-Bu bromoacetate, tert-butyl-(3R)-3-(isobutyl)succinate, and L-phenylalanine Me ester hydrochloride, showed Ki = 85, 3,000, and .apprx.100 nM for inhibition of papain, cathepsin B, and cathepsin L, resp.

IT 247209-41-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclyl peptide derivs. as cysteine protease inhibitors)

RN 247209-41-2 HCAPLUS

CN L-glycero-Hexonamide, 3,4,5,6-tetradeoxy-3-[[(1,1-dimethylethoxy)carbonyl]amino]-N-hydroxy-6-[[imino[[(2,3,6-trimethyl-4-methoxyphenyl)sulfonyl]amino]methyl]amino]-, 2-acetate, (2ξ)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	114.38	295.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-16.00	-16.00

FILE 'CAOLD' ENTERED AT 12:30:18 ON 23 JAN 2008

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

Updated Search

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

```
=> d his

     (FILE 'HOME' ENTERED AT 12:25:14 ON 23 JAN 2008)

     FILE 'REGISTRY' ENTERED AT 12:25:19 ON 23 JAN 2008
L1              STRUCTURE UPLOADED
L2            2 S L1
L3           99 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 12:29:23 ON 23 JAN 2008
L4           20 S L3
L5            1 S L4 AND LIM, Z?/AU
L6           19 S L4 NOT L5
L7            0 S L6 AND WANG, H?/AU
L8            0 S L6 AND ZHOU, Y?/AU

     FILE 'CAOLD' ENTERED AT 12:30:18 ON 23 JAN 2008

=> s l3
L9            0 L3
```

Updated Search